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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,000	05/10/2001	Takashi Osumi	046124-5005-02-US	4124

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WASHINGTON, DC 20036-5869

EXAMINER
SLOBODYANSKY, ELIZABETH

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/10/2002

6

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/852,000

**Applicant(s)**

OSUMI ET AL.

**Examiner**

Elizabeth Slobodyansky

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 8-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 9, 12 and 14 is/are allowed.
- 6) ☒ Claim(s) 8, 10, 11, 13 and 15-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/121,539.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.

- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

This application is a divisional of copending application 09/615,655.

The amendment filed concurrently with the application amending the specification to correct clerical errors, canceling claims 1-7, amending claims 8-14 and adding claims 15-20 has been entered.

Claims 8-20 are pending.

### ***Priority***

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/121,539 filed on July 24, 1998. The certified translation thereof filed in parent Application No. 09/121,539 and in the instant application.

### ***Drawings***

The drawings filed concurrently with the specification have been objected by Draftsman, please refer to the attached form PTO-948 for details.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

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enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 10, 11, 13 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8, 10, 11, 13 and 15-20 are directed to a fluorescent protein comprising the amino acid sequence set forth in SEQ ID NO:1 comprising at least mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; and Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg, respectively, and methods of use thereof. The use of "comprising at least mutations" renders the claims to encompass any fluorescent protein having any structure and any fluorescent characteristics as long as its structure comprises the above mutations.

Therefore, the claims are drawn to a genus of fluorescent proteins described by insufficient limitations on either structure or function. The specification discloses no identifying characteristics which would allow to recognize a structure as exhibiting any fluorescence. Therefore, based on the instant disclosure, it is unpredictable either a protein is a fluorescent protein. Thus, a fluorescent protein comprising the amino acid

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sequence set forth in SEQ ID NO:1 comprising at least mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; and Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg lack sufficient written description needed to practice the invention of claims 8, 10, 11, 13 and 15-20.

Claims 8, 10, 11, 13 and 15-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fluorescent protein having the amino acid sequence of SEQ ID NO:1 consisting of mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; and Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg, does not reasonably provide enablement for a fluorescent protein having the amino acid sequence of SEQ ID NO:1 comprising at least mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; and Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

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Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988).

They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 8, 10, 11, 13 and 15-20 are directed to a fluorescent protein comprising the amino acid sequence set forth in SEQ ID NO:1 comprising at least mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; and Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg. This amounts to any fluorescent protein having any structure and any fluorescent characteristics as long as its structure comprises the above mutations.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any sequence that comprises mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; or Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg because the specification does not establish:

(A) regions of the protein structure which may be modified without effecting the specific

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requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; © a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, in order to make a fluorescent protein having any amino acid sequence comprising at least mutations of Phe64Leu, Val163Ala and Ser175Gly; Tyr66His, Tyr145Phe and

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Phe64Leu; Tyr66His, Tyr145Phe, Phe64Leu and Leu236Arg; or Tyr66His, Tyr145Phe, Phe64Leu, Val163Ala, Ser175Gly and Leu236Arg in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

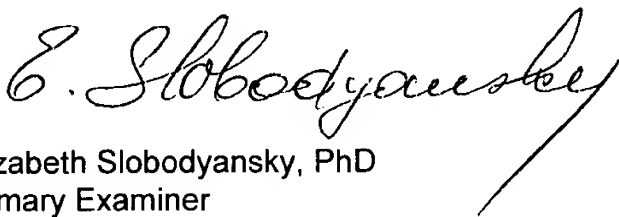
***Allowable Subject Matter***

Claims 9, 12 and 14 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.



Elizabeth Slobodyansky, PhD  
Primary Examiner

January 8, 2002